General

Guideline Title

The use of dexamethasone in patients with high grade gliomas.

Bibliographic Source(s)

Alberta Provincial CNS Tumour Team. The use of dexamethasone in patients with high grade gliomas. Edmonton (Alberta): CancerControl Alberta; 2013 Mar. 22 p. (Clinical practice guideline; no. CNS-011). [56 references]

Guideline Status

This is the current release of the guideline.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- November 6, 2013 – Low Molecular Weight Heparins: The U.S. Food and Drug Administration (FDA) is recommending that health care professionals carefully consider the timing of spinal catheter placement and removal in patients taking anticoagulant drugs, such as enoxaparin, and delay dosing of anticoagulant medications for some time interval after catheter removal to decrease the risk of spinal column bleeding and subsequent paralysis after spinal injections, including epidural procedures and lumbar punctures. These new timing recommendations, which can decrease the risk of epidural or spinal hematoma, will be added to the labels of anticoagulant drugs known as low molecular weight heparins, including Lovenox and generic enoxaparin products and similar products.

Recommendations

Major Recommendations

1. Treatment with dexamethasone is recommended for symptom relief in patients with primary high-grade gliomas and cerebral edema.
2. Following surgery, a maximum dose of 16 mg daily, administered in four equal daily doses is recommended for symptomatic patients; this protocol should ideally be started by the neurosurgeon.
3. Dexamethasone should be tapered in a manner individualized to each patient; the authors recommend one of three taper schedules:
    - Slow taper: starting with 4 mg twice daily for 7 days, then 2 mg twice daily for 7 days, then 1 mg twice daily for 7 days, then 1 mg

once daily for 7 days.
    - Fast taper: dexamethasone can be discontinued within 3 days of surgery.
    - Individualized taper: a taper schedule individualized for a specific patient as decided upon by the physician.
4. Patients who have high-grade tumours, are symptomatic, or have a poor life expectancy, can be maintained on a 0.5–1.0 mg daily dose of dexamethasone.
5. Side effects of dexamethasone are common, and increase in frequency and severity with increased dose and duration of therapy. Patients should be carefully monitored for endocrine, muscular, skeletal, gastrointestinal, psychiatric, and hematologic complications, as well as for infections and other general side effects.

Clinical Algorithm(s)

An algorithm titled "Dexamethasone Tapering Schedule for Adult Patients with High-grade Gliomas" is provided in the original guideline document.

Scope

Disease/Condition(s)

High-grade glioma symptoms

- Cerebral edema
- Increased intracranial pressure

Guideline Category

Management

Prevention

Treatment

Clinical Specialty

Neurological Surgery

Neurology

Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To review the evidence for the use of dexamethasone in patients with high-grade gliomas
- To describe the management of side effects associated with dexamethasone use in this patient population

- To document the recommendations of the Alberta Provincial CNS Tumour Team for the use of dexamethasone in patients with high-grade gliomas

Target Population

Adult patients with primary high-grade gliomas

Interventions and Practices Considered

1. Dexamethasone therapy
2. Individualized tapering schedules of dexamethasone
3. Low-dose maintenance therapy
4. Monitoring for endocrine, muscular, skeletal, gastrointestinal, psychiatric, and hematologic complications, as well as for infections and other general side effects

Major Outcomes Considered

- Risk for and incidence of complications of dexamethasone therapy, including:
  - Hyperglycemia
  - Muscular complications (e.g., steroid myopathy)
  - Skeletal complications (e.g., bone loss)
  - Gastrointestinal (GI) complications (e.g., peptic ulcer and GI hemorrhage, bowel perforation)
  - Psychiatric complications
  - Infections (e.g., *Pneumocystis jirovecii* pneumonia, formerly *Pneumocystis carinii* pneumonia or PCP, and Candida mucositis and esophagitis)
  - Hematologic complications (e.g., venous thromboembolism)
  - Cardiovascular complications
- Effectiveness of preventive and therapeutic interventions for dexamethasone-related complications

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Searches of Unpublished Data

Description of Methods Used to Collect/Select the Evidence

Research Questions

Specific research questions to be addressed by the guideline document were formulated by the guideline lead(s) and Knowledge Management (KM) Specialist using the PICO question format (patient or population, intervention, comparisons, outcomes).

Guideline Questions

- When should dexamethasone be considered in adult patients with high-grade gliomas?
- What are the optimal dose ranges?

- What is the optimal schedule for dexamethasone tapering?
- What are the most common adverse events associated with dexamethasone therapy, and how are they best managed?

Search Strategy

Medical journal articles were searched using the Medline (1948 to Nov Week 3 2012), PubMed (1950-Nov 2012), Cochrane Database of Systematic Reviews (2005 to Nov 2012), and CINAHL (1982 to Nov 2012) electronic databases. Search terms included: dexamethasone OR glucocorticoids OR corticosteroids OR decadron OR adrenal cortex hormones AND brain tumour or glioma OR high-grade glioma OR brain neoplasm. The reference lists of relevant articles were hand searched for additional articles. In addition to the Guideline Clearinghouse database, the websites of the following guideline developers were searched for relevant content: the American College of Radiology (ACR), the Australian Cancer Network, the British Columbia Cancer Agency (BCCA), Cancer Care Ontario (CCO), the European Society for Medical Oncology (ESMO), the National Comprehensive Cancer Network (NCCN), and the National Institute for Health and Care Excellence (NICE). A search of the grey literature was also conducted using Google and Google Scholar. The patient population was limited to adolescents and adults; there were no limitations by date, publication type, or study design. The literature search resulted in eight publications which were used to formulate the final recommendations addressing the first three guideline questions. To address the fourth guideline question, a systematic review of the literature was carried out incorporating the MeSH terms listed above in combination with the following keywords: hyperglycemia, myopathy, osteoporosis, avascular necrosis, peptic ulceration, bowel perforation, anxiety, irritability, insomnia, mania, psychosis, depression, seizures, infections, *Pneumocystic jirovecii* pneumonia, candidiasis, venous thromboembolism, hypertension, cardiovascular complications, weight gain, Cushingoid, hirsutism, fragile skin, and skin complications.

Number of Source Documents

The literature search resulted in eight publications which were used to formulate the final recommendations addressing the first three guideline questions.

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Evidence was selected and reviewed by a working group comprised of a medical oncologist, a pharmacist, and a Knowledge Management (KM) specialist, with input from an endocrinologist. A detailed description of the methodology followed during the guideline development process can be found in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field).

Evidence Tables

Evidence tables containing the first author, year of publication, patient group/stage of disease, methodology, and main outcomes of interest are assembled using the studies identified in the literature search. Existing guidelines on the topic are assessed by the KM Specialist using portions of the Appraisal of Guidelines Research and Evaluation (AGREE) II instrument (http://www.agreetrust.org) and those meeting the minimum requirements are included in the evidence document. Due to limited resources, the Guideline Utilization Resource Unit (GURU) does not regularly employ the use of multiple reviewers to rank the level of evidence; rather, the methodology portion of the evidence table contains the pertinent information required for the reader to judge for himself the quality of the studies.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Formulating Recommendations

The working group members formulated the guideline recommendations based on the evidence synthesized by the Knowledge Management (KM) Specialist during the planning process, blended with expert clinical interpretation of the evidence. As detailed in the Guideline Utilization Resource Unit Handbook (see the "Availability of Companion Documents" field), the working group members may decide to adopt the recommendations of another institution without any revisions, adapt the recommendations of another institution or institutions to better reflect local practices, or develop their own set of recommendations by adapting some, but not all, recommendations from different guidelines.

The degree to which a recommendation is based on expert opinion of the working group and/or the Provincial Tumour Team members is explicitly stated in the guideline recommendations. Similar to the American Society of Clinical Oncology (ASCO) methodology for formulating guideline recommendations, the Guideline Utilization Resource Unit (GURU) does not use formal rating schemes for describing the strength of the recommendations, but rather describes, in conventional and explicit language, the type and quality of the research and existing guidelines that were taken into consideration when formulating the recommendations.

The working group drafted the recommendations and guideline, and distributed this document for review and comment to members of the Alberta Provincial CNS Tumour Team (N=30) via an anonymous electronic survey. The response rate was 33%.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Internal Peer Review

Description of Method of Guideline Validation

The final guideline was reviewed and endorsed in February 2013 by the Alberta Provincial CNS Tumour Team.

When the draft guideline document has been completed, revised, and reviewed by the Knowledge Management Specialist and the working group members, it is sent to all members of the Provincial Tumour Team for review and comment. This step ensures that those intended to use the guideline have the opportunity to review the document and identify potential difficulties for implementation before the guideline is finalized. Depending on the size of the document, and the number of people it is sent to for review, a deadline of one to two weeks will usually be given to submit any feedback. Ideally, this review will occur prior to the annual Provincial Tumour Team meeting, and a discussion of the proposed edits will take place at the meeting. The working group members will then make final revisions to the document based on the received feedback, as appropriate. Once the guideline is finalized, it will be officially endorsed by the Provincial Tumour Team Lead and the Executive Director of Provincial Tumour Programs.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Appropriate use of dexamethasone in patients with high-grade gliomas
- Appropriate management of dexamethasone-associated complications

Potential Harms

- There is a high-rate of side-effects associated with prolonged dexamethasone use, as well as a risk of suppression of the hypothalamic-pituitary-adrenocortical (HPA) axis. All patients should be observed for symptoms adrenal insufficiency if dexamethasone is discontinued, and advice from an endocrinologist should be sought if needed.
- The most common complications of steroid therapy are listed in Table 2 in the original guideline document. Detailed information regarding endocrine, muscular, skeletal, gastrointestinal, psychiatric, and hematologic complications, as well as infections and other general side effects, is provided in the original guideline.

Contraindications

Contraindications

- Teriparatide for glucocorticoid-induced osteoporosis is contraindicated in patients with active malignancy.
- Tricyclic antidepressants are not recommended in patients with brain tumours experiencing psychiatric effects of steroids, as they may confound the problem.

Qualifying Statements

Qualifying Statements

The recommendations contained in this guideline are a consensus of the Alberta Provincial CNS Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

Implementation of the Guideline

Description of Implementation Strategy

- Present the guideline at the local and provincial tumour team meetings and weekly rounds.
- Post the guideline on the Alberta Health Services Web site.
- Send an electronic notification of the new guideline to all members of CancerControl Alberta.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

Alberta Provincial CNS Tumour Team. The use of dexamethasone in patients with high grade gliomas. Edmonton (Alberta): CancerControl Alberta; 2013 Mar. 22 p. (Clinical practice guideline; no. CNS-011). [56 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Mar

Guideline Developer(s)

CancerControl Alberta - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

CancerControl Alberta

Guideline Committee

Alberta Provincial CNS Tumour Team

Composition of Group That Authored the Guideline

Members of the working group include a medical oncologist, a pharmacist, a Knowledge Management (KM) specialist, and an endocrinologist. Members of the Alberta Provincial CNS Tumour Team include medical oncologists, pediatric oncologists, neuro-oncologists, radiation oncologists, surgical oncologists, nurses, pathologists, and pharmacists.

Financial Disclosures/Conflicts of Interest

Participation of members of the Alberta Provincial CNS Tumour Team in the development of this guideline has been voluntary and the authors have not been remunerated for their contributions. There was no direct industry involvement in the development or dissemination of this guideline. CancerControl Alberta recognizes that although industry support of research, education and other areas is necessary in order to advance patient care, such support may lead to potential conflicts of interest. Some members of the Alberta Provincial CNS Tumour Team are involved in research funded by industry or have other such potential conflicts of interest. However the developers of this guideline are satisfied it was developed in an unbiased manner.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the Alberta Health Services Web site .

Availability of Companion Documents

The following is available:

- Guideline utilization resource unit handbook. Edmonton (Alberta): CancerControl Alberta; 2013 Jan. 5 p. Electronic copies: Available from the Alberta Health Services Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on August 12, 2014. The information was verified by the guideline developer on September 22, 2014.

Copyright Statement

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